What is normal bone health? A bioarchaeological perspective on meaningful measures and interpretations of bone strength, loss, and aging

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[Correction added on 4th August 2021, after first online publication. A word Bioarcheological has been updated as Bioarchaeological globally.]

Abstract
Bioarchaeological (the study of archeological human remains together with contextual and documentary evidence) offers a unique vantage point to examine variation in skeletal morphology related to influences such as activity, disease, and nutrition. The human skeleton is composed of a dynamic tissue that is forged by biocultural factors over the entire life course, providing a record of individual, and community history. Various aspects of adult bone health, particularly bone maintenance and loss and the associated skeletal disease osteoporosis, have been examined in numerous past populations. The anthropological study of bone loss has traditionally focused on the signature of postmenopausal aging, costs of reproduction, and fragility in females. The a priori expectation of normative sex-related bone loss/fragility in bioanthropological studies illustrates the wider gender-ideological bias that continues in research design and data analysis in the field. Contextualized data on bone maintenance and aging in the archeological record show that patterns of bone loss do not constitute predictable consequences of aging or biological sex. Instead, the critical examination of bioarchaeological data highlights the complex and changing processes that craft the human body over the life course, and calls for us to question the ideal or “normal” range of bone quantity and quality in the human skeleton, and to critically reflect on what measures are actually biologically and/or socially meaningful.

1 INTRODUCTION
Aging in humans is the product of cumulative changes in biology and physiology over the life cycle interweaved with environmental and social processes. Globally, human populations are growing exponentially older due to increasing life expectancy and falling fertility levels, coupled with a reduction in overall population size in many countries (United Nations, 2019). In 2018, for the first time in history, persons aged 65 or above outnumbered children under 5 years of age, and the number of persons aged 80 years or over is projected to triple, from 143 million in 2019 to 426 million in 2050 (United Nations, 2019). While the individual experience of aging is variable, the increased susceptibility to and frequency of disease, frailty, or disability with age is a growing concern in industrialized populations.

Advancing age is a major risk factor for a number of chronic diseases in humans. Osteoporosis is one of the diseases most commonly associated with aging. Osteoporosis is clinically defined as abnormal bone loss and its most severe form is accompanied by the presence of fragility fractures that occur with only minimal trauma (Birnbaum, 1992; Center & Eisman, 1997; Melton, 2003;...
Mundy, 1995; Ross et al., 1999). Bone loss and increase in fracture risk occurs in both sexes with age, however, women can suffer greater overall bone loss due to the compounded effect of menopausal bone loss with aging (Khosla & Riggs, 2005). Using data from the National Health and Nutrition Examination Survey III (NHANES III), the National Osteoporosis Foundation (NOF) has estimated that more than 9.9 million Americans have osteoporosis and an additional 43.1 million have low bone density (defined as osteopenia) (Wright et al., 2014), and worldwide osteoporosis is estimated to affect 200 million women (Kanis, 2007). To get a sense of the immensity of those affected, about half of women and one quarter of men over age 50 will break a bone in their remaining lifetime. For women, this is equivalent to the risk of getting cancers of the breast, ovaries, and uterus combined, while for men the risk is equivalent to getting prostate cancer (Cosman et al., 2014). Osteoporosis-related fractures are not only associated with significant morbidity and mortality (Cauley et al., 2000; Center et al., 1999; Kanis et al., 2003) and high economic impact for treatment (Johnell, 1997; Johnell et al., 2004; Johnell & Kanis, 2005, 2006) but also cause a significant reduction in quality of life (Cockerill et al., 2004).

While there has been significant focus on chronic diseases like osteoporosis with aging, we have little understanding of the evolution of aging in our species or the aging process itself, particularly outside of industrialized human populations (Emery Thompson et al., 2020). In order to better understand the range of environmental and social factors that shape human aging, studies have attempted to examine aspects of the aging process and health in non-industrialized populations. For example, studies of bone density and loss in rural Gambian women with low calcium intake and natural fertility patterns (Prentice et al., 1993; Prentice & Bates, 1993) have shown significant loss of bone mass with lactation, that is however recovered and restored in later life (Jarjou et al. and one; Sawo et al., 2013). The recent studies that have examined bone loss and health in small-scale subsistence groups, have examined human groups with energy-limitations and natural fertility patterns, in order to focus on “trade-off” consequences of bone aging. In this work postmenopausal bone loss is framed as an example of antagonistic pleiotropy, in which traits that are beneficial to earlier reproductive life become deleterious when compounded with senescence (Galloway, 1997), or as the updated “disposable soma” theory of aging that makes the further argument that mothers trade off their own somatic bodily maintenance as an investment in offspring (Kirkwood & Rose, 1991). For example, a study of bone density in a forager-horticulturalist population, the Tsimane of Bolivia, found postmenopausal women with high parity, short birth spacing, and early age at first birth to be associated with reduced bone density, that the authors attribute to energetic constraints together with high pathogen burden (Stieglitz et al., 2015; Stieglitz et al., 2016). However, in contrast, a study of bone density among the Shuar forager-horticulturalist women of Amazonian Ecuador did not find an association between high parity and lactation duration and postmenopausal bone density (Madimenos, 2015; Madimenos et al., 2011; Madimenos et al., 2012; Madimenos et al., 2020). These contrasting studies underscore the plasticity and variation in bone health, and demonstrate a need for further studies of bone loss in small-scale societies that have very different lifestyle and life history variables at play as compared to industrialized populations.

This variation in bone loss, and the complex relationship between bone aging and biological sex, has also been observed in studies of prehistoric and historic populations. The study of bone loss in the past offers a unique perspective into the natural history of bone health and aging with an ability to examine populations from a variety of biosocial contexts that differ from the majority of contemporary industrialized societies. As such, there have been numerous studies of bone loss in the past from a variety of geographic locations and time periods. While low bone mass in adulthood has been noted in a large number of prehistoric and historic samples (Agarwal, 2018), the normative pattern of postmenopausal bone loss and fragility seen in contemporary industrial women is not always seen in the past (Agarwal, 2012; Agarwal et al., 2003; Agarwal & Grynpas, 1996, 2009; Nelson et al., 2014; Robling & Stout, 2004). Instead, bone loss is often seen at younger ages and in both sexes (Agarwal, 2012; Agarwal & Grynpas, 1996, 2009; Brodholt et al., 2021; Ekenman et al., 1995; Holck, 2007; Lees et al. 1993; Weaver, 1998), is often very similar between the sexes (Bickley, 2002; Cho & Stout, 2011; Ekenman et al., 1995; Holck, 2007; Robling & Stout, 2004), and fragility fractures also seem to occur at far lower frequencies than in modern populations (Agarwal, 2008; Ives et al., 2017; Madimenos, 2015).

However, studies of bone loss in industrialized populations, small-scale societies, and archeological populations have all been designed within a culturally shaped normative view of bone and fragility. The result is that interpretations of bone loss in females have focused on what is considered the traditional signature of normative aging with diminished reproductive capabilities and/or costs of reproduction in adulthood. The goal of this article is not to argue that aging or menopause is unrelated to bone loss. Clearly, bone loss occurs in most vertebrates as they age, and humans demonstrate bone loss with loss of sex steroids (Draper, 1994). Instead, the goals of this article are to question the ideal or “normal”
range of bone quantity and quality in the human skeleton, to critically reflect on which measures of bone loss in the different parts of the skeleton are actually biologically and/or socially meaningful, and to call for greater consideration of the cumulative and fluid biocultural influences on the skeleton over the life course beyond sex and age. This article begins with a contextualization of how bone works and the normative pattern of bone loss in contemporary industrialized populations, and a brief discussion of the complex and synergistic factors that influence bone growth and aging. A review will then be given of the studies of bone maintenance and aging in the archeological record that demonstrate that patterns of bone loss do not constitute predictable consequences of aging or biological sex. Finally, the critical examination of bioarchaeological and evolutionary data illustrate the dynamic processes that construct the human body and skeleton over the life course, and sets the stage to move beyond the expectation of female fragility.

2 | BACKGROUND

2.1 | How bone works

A fundamental aspect of the human skeleton is its remarkable ability to grow, maintain, and renew itself at the tissue level. The primary mode of bone growth in the immature skeleton is called modeling, where bone is formed and then soon resorbed in different locations, although bone modeling can occur on some bone surfaces in adulthood (Parfitt, 2003). In the adult skeleton bone remodeling is the primary mode of maintenance and replacement, where bone tissue is systematically resorbed and then replaced in the same area (Parfitt, 2003). Although, ideally, bone remodeling replaces an equal amount of bone that it removes, under many circumstances bone remodeling results in a net loss of bone. Bone remodels for various reasons. Bone tissue in areas of the skeleton that serve a metabolic function will be remodeled during calcium homeostasis and the production of blood cells in the body (Parfitt, 2003). Bone will also remodel in times of intense physiological demands for calcium such as growth, pregnancy, and lactation (Frost, 2003; Parfitt, 2003). But another function of the skeleton and bony tissue is to resist mechanical loads, and like other materials that bear dynamic loads, over time the material accumulates fatigue damage. As such, remodeling also serves to maintain or repair bone tissue material (Currey, 2003; Martin, 2003; Parfitt, 2003). During life, the structure of the skeleton, at the macroscopic and microscopic levels, can change through modeling and remodeling in response to mechanical stimulation or stress in order to tolerate the effects of activity at the tissue level (Martin, 2003). In this sense, bone is literally able to “adapt” to mechanical loading sensed through its living bone cells (Martin, 2003). This means that changes and influences during growth, nutrition, activity, or disease can alter the shape and amount of bone tissue, and we can quantify these through the study of bone morphology, density, microstructure, and markers of bone turnover.

A second fundamental aspect of the human skeleton, is that there are two kinds of bone tissue, and that distribution and metabolic activity of these tissues differ across the skeleton. Twenty percent of the human skeleton is trabecular bone while 80% is cortical bone (Eriksen et al., 1994). However, the majority of bone remodeling and turnover (80%) occurs in the smaller amount of trabecular bone (Cosman et al., 2014; Eriksen et al., 1994). Both cortical bone and trabecular bone have different surfaces on which bone remodeling occurs. For example, long tubular bones (long bones) found in many parts of the skeleton, have an inner endosteal surface and also outer periosteal surface where remodeling occurs, but also have remodeling occurring within the cortical tissue on the intracortical surface. In contrast, trabecular tissue that makes up the spongy inside of bones (such as in the ends of long bones and the vertebral bodies) has abundant honeycomb endosteal surfaces of interconnected trabecular spicules where remodeling occurs (Seeman, 1997; Szulc & Seeman, 2009).

It is key to note that remodeling on these surfaces can occur in tandem or independently, and can differ across the life cycle and between sexes (Farr & Khosla, 2015; Szulc & Seeman, 2009). In adults before the age of 65, most of the surface area available for remodeling is in the trabecular tissue, and as such early bone loss will occur here, while in later age the increased porosity and endosteal surface area results in significant intracortical remodeling (Osterhoff et al., 2016). While studies of bone loss in one area of the body are used to estimate or reflect overall bone strength or fracture risk, prediction is not equal across all populations or between individuals (Choksi et al., 2018; Hunter & Sambrook, 2000; Leslie et al., 2007). In clinical settings, bone loss and fracture risk are primarily assessed with noninvasive methods in areas such as the spine, hip, and forearm that have different ratios of trabecular and cortical tissue (Hunter & Sambrook, 2000). While bone loss in different skeletal areas is usually correlated (Hunter & Sambrook, 2000), loss of bone tissue will have different consequences to bone health depending on where it occurs in the skeleton (Farr & Khosla, 2015).

Finally, during growth the skeleton accrues bone in order to grow in length, breadth, mass, and volumetric...
density (Cooper et al., 2006; Parfitt, 1994). The maximal amount of bone accrued, or peak bone mass, occurs after the fusion of the long bones, thus at different times in males and females. The exact age of peak bone mass differs at various skeletal sites, but is thought to generally occur by 20–30 years of age (Cosman et al., 2014). As such, bone mass in old age, is dependent not just on how much bone is lost later in life, but also on how much peak bone was gained during growth in the first place. Bone growth and peak bone mass are highly sensitive and influenced by several factors including nutrition, genetics, and disease.

2.2 | Defining normal bone loss and aging

The normative statistical curve of the expected loss of bone with age (normally measured as bone mass) is clinically well established and ubiquitous in the literature (Figure 1). These curves emphasize that bone density normally peaks at young age and that both sexes lose bone with age, and typically show women to lose bone mass more rapidly than men with a subsequent greater net loss. Bone loss is a “silent disease” without symptom of pain or discomfort until fracture. Clinically, the gold standard for the diagnosis of osteoporosis is given through the assessment of low bone mineral density (BMD) determined by dual-energy X-ray absorptiometry (DEXA) (Center & Eisman, 1997). Osteoporosis is diagnosed when bone mineral density is less than or equal to 2.5 SD below that of young (30–40-year-old) adult women derived from a healthy reference population, translated as a T-score (World Health Organization, 2003). This T-score cutoff and definition is the international reference standard for osteoporosis diagnosis, and the biomedical standard to categorize which women have normal bone and which are potentially pathological. Despite this accepted standard, several limitations of the WHO reference standards have been identified. The recognition of additional risk factors, aside from BMD T-scores, such as age, gender, or previous fracture history has led to the creation and use of predictive models such as the Fracture Risk Assessment Tool (FRAX) to improve fracture prediction over the BMD T-score method alone (Wu et al., 2020). Further, the T-score standard was initially created for postmenopausal Caucasian women, and even with subsequent adjustments for race and ethnicity, fracture risk prediction in diverse populations is problematic (Wu et al., 2020). There has also been a push to better characterize what the normative curves of bone loss look like in diverse ethnic populations (Barrett-Connor et al., 2005; Zengin et al., 2015) and to appreciate the ethnic disparities that exist in the screening, diagnosis, and treatment of osteoporosis (Cauley, 2011). Why different ethnic groups and populations vary globally in fracture risk is complicated and not clear, and is not related to “racial” genetic differences alone. Additional risk factors for fracture along with BMD that have been identified include bone geometry, fall rates, fracture history, and medication use (Cauley, 2011). The reality is that while the biomedical standards are routinely used to define what is normal bone quantity and bone loss, they are not easily applicable to all men and women within Western populations for which they were devised, let alone populations globally.

Further, while BMD/bone mass correlates with risk of fracture, there are a number of additional factors that significantly contribute to bone strength that are actually independent of bone mass (Augat & Schorlemmer, 2006; Burr, 2004; Heaney, 1992; Hernandez & Keaveny, 2006; Turner, 2002; Watts, 2002). Bone strength and fracture risk are influenced by bone geometry, trabecular and cortical microarchitecture, and bone material properties such as porosity, mineralization, and collagen crosslinks, often grouped together as “bone quality” features. While the term “bone quality” includes a broad range of characteristics of bone tissue that are difficult to separate from measures of BMD (Sievänen et al., 2007), there is considerable in vitro evidence that these aspects of bone structure and bone matrix play a significant role in bone fragility with aging and disease (Agarwal & Grynpas, 1996; Burr & Turner, 1999; Compston, 2006; Cooper, 1993; Grynpas, 2003; Heaney, 1992; Osterhoff et al., 2016; Seeman & Delmas, 2006; Watts, 2002).
However, the risk of osteoporosis in the clinical setting is defined and focused on bone mass only, primarily because there are limited ways to measure most aspects of bone quality in vivo (Kanis, 2002). This has recently started to change with the ability to use state-of-the-art 3D imaging such as volumetric QCT (vQCT), high-resolution CT (hrCT), high-resolution MR (hrMR) (Abel et al., 2013; Brandi, 2009), and high-resolution peripheral quantitative computed tomography (HR-pQCT) (Boutroy et al., 2005; Whittier et al., 2020) in the clinical setting. Tools such as quantitative ultrasonography (qUS) also offer a portable alternative to absorptiometry that allows the assessment of bone quality along with bone density in remote settings such as rural populations (Knapp, 2009; Lee et al., 2021; Madimenos et al., 2011; Stiegitz et al., 2016), although there has been some question of the correlation of qUS measures with absorptiometric measures of BMD (Faulkner et al., 1994; Nguyen et al., 2021). While these newer noninvasive clinical methods do not account for all aspects of bone tissue material changes with age, they do promise more accurate assessments of fracture risk for individual patients and assessment of “whole bone strength” (Currey, 2001; Sievänen et al., 2007). A more holistic understanding of what defines normative bone loss requires the continued study of bone density, (micro)structure and bone material properties across the tissue envelopes (trabecular and cortical) of the skeleton, and a consideration of how these differ over the life cycle.

### 2.3 The etiology of bone loss and fragility

Primary osteoporosis is clinically divided as postmenopausal (type I) or age-related (type II) osteoporosis. Type I postmenopausal osteoporosis occurs with a rapid phase of bone loss due to the loss of ovarian estrogen and changes in progesterone. This results in an increase in bone turnover, and tends to affect primarily trabecular tissue in locations such as the vertebrae or distal forearm, with associated increase in fracture risk in these locations. Alternatively, type II age-related osteoporosis is seen in both sexes typically after the age of 70 (Khosla & Riggs, 2005). Uncoupled remodeling, where resorption exceeds formation, results in bone loss in both trabecular and cortical surfaces that can result in fractures at the femoral neck, vertebrae, proximal humerus, and proximal tibia (Riggs et al., 1991). Age-related bone loss is compounded by declining sex steroids (in both sexes), and is also related to increases in serum PTH that results in secondary hyperparathyroidism that has multiple etiologies including vitamin D deficiency (Khosla & Riggs, 2005). This may result from age-related reduction in vitamin D synthesis or resistance to vitamin D activity (Kanis, 1994; Grynpas, 2003). Finally, a reduction in key paracrine growth factors or circulating growth hormones also likely play a role in age-related loss of bone (Khosla & Riggs, 2005). That bone loss and risk of fracture with aging varies across human populations, both in the past and present, should not be surprising when the etiology of bone loss is considered. While bone loss is clearly linked with age and postmenopausal hormonal changes, bone loss has a multifactorial etiology, and the risk of developing osteoporosis is mediated by many independent and synergistic factors. For example, factors such as genetics, ethnicity, nutrition, physical activity, parity, and lactation are just some of the strong influences on bone maintenance (Nelson & Villa, 2003; Office of the Surgeon General, 2004; Ralston, 2005; Sowers & Galuska, 1993; Stevenson et al., 1989; Ward et al., 1995; Wilsgaard et al., 2009). Dietary calcium, protein intake, and vitamin D have all been discussed in the literature as likely important in the evolution and maintenance of the human skeleton (Nelson et al., 2014). Calcium and vitamin D, in particular, are intricately linked in bone metabolism, and deficiencies in either are well known to have negative consequences for skeletal maintenance (Heaney & Weaver, 2005). The majority of calcium is stored in the skeleton, and the body can draw as needed on this reservoir of skeletal calcium to maintain homeostasis (Heaney et al., 2006). If the diet does not provide enough calcium the body resorts to breaking down bone to fulfill its needs, potentially leading to conditions of osteopenia and osteoporosis (Heaney & Weaver, 2005). Vitamin D also plays a role in mediating the absorption of calcium in the intestines. When calcium and vitamin D intakes are low, there is a reduction in the absorption of calcium, which causes circulating calcium levels to drop. This in turn triggers an increase in PTH (parathyroid hormone) secretion, which in turn leads to bone resorption (Dawson-Hughes, 2003). As such, both long-term calcium and/or vitamin D deficiency can lead to bone loss, and in many instances, osteoporosis may actually be a consequence of sub-clinical vitamin D deficiency (Heaney et al., 1999; Parfitt, 1990; Vieth, 2003).

While it is well established that bone tissue responds to mechanical loading, it is unclear what type and level of physical activity or exercise is needed to affect bone mass and more importantly bone strength into adulthood. The negative effect on bone density with disuse such as micro-gravity in space (Turner, 2000; Vico et al., 2000) or prolonged bed rest (Heaney et al., 2006; Zerwekh et al., 1998) is well known, but the long-term effects of exercise and strain are less clear from clinical studies. While there is substantial evidence that exercise can increase BMD/mass...
during growth and development, particularly during adolescence, exercise seems to have less impact on the adult skeleton (Pearson & Lieberman, 2004; Rittweger, 2006). It has been argued that the ideal “window of opportunity” for the skeleton to grow large and robust bones is during the acquisition of peak bone mass (Pearson & Lieberman, 2004). Although some high biomechanical activity may still be effective at older ages (Rittweger, 2006), there appear to be limited effects on bone mass and geometry in adults with increased exercise in clinical studies (Bergmann et al., 2010). Further, while there has been substantial research on the effect of mechanical loading on cortical bone remodeling, bone mass, and mineral density during growth, less is known about how mechanical loading changes aspects of bone material properties and fracture risk in humans due to limitations of in vivo assessment (Hart et al., 2017).

Finally, reproductive behaviors also play a role in female bone maintenance. While pregnancy and lactation are well established to be high bone turnover states, the long-term effect of pregnancy and lactation on bone loss and fragility in humans is not clearly understood. Studies of the effects of pregnancy on bone have found conflicting results (Cross et al., 1995; Drinkwater & Chesnut 3rd., 1991; Kent et al., 1993; Naylor et al., 2000; Saliari & Abdollahi, 2014; Sowers et al., 1992; Winter et al., 2020), but epidemiological evidence suggests that parity may decrease fracture risk and could increase bone density (Fox et al., 1993; Murphy et al., 1994; Sowers et al., 1992). Further, longitudinal studies indicate that while bone loss occurs during initial lactation (Affinito et al., 1996; Chan et al., 1982; Drinkwater & Chesnut 3rd., 1991; Hayslip et al., 1989; Kent et al., 1993; Lamke et al., 1977; Lopez et al., 1996; Sowers, 1996; Sowers et al., 1993, 1995), recovery of bone occurs with extended lactation and during weaning (Affinito et al., 1996; Arreola et al., 2015; Grizzo et al., 2020; Kent et al., 1993; Lenora et al., 2009; Lopez et al., 1996; Pearson et al., 2004; Sowers, 1996; Sowers et al., 1993, 1995).

While the normative age-related drop in bone mass is observed in populations that mirror reference standards, populations with significant deviation in genetic structure, diet, activity patterns, or reproductive behavior can very easily add complexity to an individual’s trajectory of bone maintenance and ultimate fracture risk. As discussed earlier, these environmental and behavioral influences also act differentially across the bone tissues and remodeling surfaces. To complicate things further, current experimental and epidemiological studies demonstrate that bone loss and fragility accompanying old age is tied to the influences on bone maintenance early in growth and development (Cooper et al., 2002, 2006; Gale et al., 2001; Javaid et al., 2006), and recent life course approaches have emphasized the importance of understanding the interrelationships and joint cumulative contributions of different factors (e.g., genetics, diet, exercise, reproduction) to bone development, maintenance, and loss over the entire lifecycle (Agarwal et al., 2004; Agarwal & Beauchesne, 2011; Fausto-Sterling, 2005; Weaver, 1998).

The constraints and plasticity of human bone aging are the result of the long evolutionary history of our species. As such, it is difficult to fully understand bone loss with age in modern industrialized populations that have lifestyles and environments that are dramatically different from those experienced during much of our (pre)historic past. There have been numerous studies of bone loss in past populations, and these studies offer us a key temporal window to examine how bone aging occurs in populations with variable life history traits and biosocial experiences. A critical examination of bone loss and fragility data from these samples highlight the challenges in reconstructing the interrelated influences on bone maintenance, and emphasize the importance of life course perspectives on bone loss and fragility.

## 3 | VARIATION AND PLASTICITY: THE ARCHEOLOGICAL PERSPECTIVE

### 3.1 | Temporal and evolutionary studies of bone robusticity

In recent years there has been increasing interest to examine temporal trends in bone quantity and strength in humans, particularly from a biomechanical approach. Studies of paleontological and archeological remains have demonstrated a gracilization of the modern human skeleton, with a decline in overall skeletal strength relative to body size over the course of human evolution, that has become progressively steeper in recent millennia related to increased sedentism (Holt, 2003; Ruff, 2005; Shaw & Stock, 2013). For example, Ruff et al. (2015) found a decline in mediolateral bending strength in upper and lower limb long bones in a large sample of European skeletons dating from the Upper Paleolithic (about 40 000 years ago) to the 20th century, interpreted as reflecting the decline in mobility and activity with the shift from foraging toward food production (Ruff et al., 2015). Similarly, a study of prolonged change in lower limb cortical morphology in Central Europe from the initial spread of agriculture (~5300 BC) through to the early Medieval period found a temporal change of declining tibial bone strength in males and gradual declines in tibial loading in females (Macintosh...
et al., 2014a). It is unclear if this trend in human evolution is primarily the result of decreased mechanical stimulus during life and/or the result of direct selection for gracile and perhaps lighter skeletons as the selection pressure for more robust skeletons was lost with sedentary lifestyles (Chirchir et al., 2015; Martin, 2003).

These findings in cortical bone are also consistent with recent studies of temporal changes in trabecular bone tissue in humans. For example, Ryan and Shaw (2015) examined human populations representing foragers and sedentary agriculturalists, finding forager groups to have higher bone volume and thicker trabeculae that were interpreted as likely resulting from high physical activity at a young age. Similarly, Chirchir et al. (2015) found low trabecular density (bone volume fraction) in limb epiphyses in recent modern humans as compared with extinct hominins, that is also interpreted as related to increased sedentism. A second study by Chirchir et al. (2017) of trabecular bone in upper and lower limbs, found similar temporal patterns of lower trabecular bone density in the sedentary populations, although more variation in the upper limb elements. Similarly, a study of trabecular bone in the humerus of Neolithic farmers found greater trabecular bone volume as compared with more recent humans, also attributed to more strenuous activities in the Neolithic (Scherf et al., 2016). A comparative study of trabecular bone structure in the lower limb (femur and tibia) from a highly mobile foraging population and two sedentary agriculturalist samples from North America and Nubia, also found a positive correlation between trabecular bone volume and greater terrestrial mobility (Saers et al., 2016). A subsequent study by Doershuk et al. (2019) examined trabecular bone in both the lower (femur) and upper limb (humerus) using some of the same samples along with additional modern human samples, and also found that reduced trabecular bone in both locations corresponded with reduced inferred subsistence activity levels. Saers et al. (2019) have also found greater inferred terrestrial mobility to be associated with greater trabecular bone volume in the bones of the foot, and a study of trabecular bone across the human hand found greater site-specific bone volume in the hands of a forager skeletal samples as compared with later agricultural/industrial groups (Stephens, Kivell, Pahr, Hublin, and Skinner, 2018).

Evolutionary studies have also been used to frame osteoporosis as a modern “mismatch” disease that is the result of our historical shift toward sedentary lifestyles that no longer reflect the biomechanical environment that the human skeleton evolved in (Gurven & Lieberman, 2020; Kralick and Zemel, 2020; Latimer, 2005; Lieberman, 2014; Ruff, 2006; Ryan & Shaw, 2015; Saers et al., 2017; Trevathan, 2010; Wallace et al., 2015). The suggested implication is that modern humans, particularly females, are prone to bone loss and fragility if bone maintenance is further compromised from influences such as reproductive stress, poor diet, or pathogen load. However, evolutionary studies have examined temporal trends in bone quantity and biomechanical measures of strength primarily in mid-adulthood, and there has been limited consideration of variation in gender-related behaviors or how these influences may have played out over the life cycle. While sex differences in long bone robusticity and trabecular volume have been considered in the most recent studies, reported results have varied. For example, studies of trabecular structure in sedentary agricultural populations vs. foragers have found no sex difference in trabecular bone volume or density (Chirchir et al., 2015; Doershuk et al. 2019; Saers et al., 2016), greater trabecular density observed only in Neolithic males as compared to females, but not modern males and females (Scherf et al., 2016), or greater trabecular bone volume in historic females as compared to males, counter to predictions (Saers et al., 2017). Since studies of diachronic trends in bone robusticity have focused on large scale changes over time through examining changes in a large number of differing temporal populations, the sample sizes within each population are also generally too small to detect differences between the sexes (e.g., Chirchir et al., 2015; Saers et al., 2016; Scherf et al., 2016; Stephens et al. 2018). Further, changes in bone robusticity do not consider change in robusticity with age, opting to only include young/mid-age adults and/or explicitly not include individuals over 45 years of age (Chirchir et al., 2017; Macintosh et al., 2014a, 2014b; Ruff et al., 2015; Saers et al., 2016; Scherf et al., 2016), or not even use age as a covariate estimate in statistical models (Saers et al., 2019). For example, while the study of upper limb robusticity and asymmetry (indicative of handedness and task specialization) by Macintosh et al. (2014b) and a more recent study by Sládek et al. (2016) did have sufficient sample size to examine sex differences in limb loading related to gendered differences in manipulative behaviors, these studies do not consider age-related changes or bone loss. While these evolutionary studies clearly demonstrate a general decrease or changes in skeletal robusticity over time correlated with subsistence mobility or technological innovation, without sufficient sample sizes and wider range of age distributions, they are not able to detect or make meaningful interpretations of age- or sex-related bone loss. However, recent comparative studies of cortical long bone robusticity in a variety of modern populations have found varying patterns of sexual dimorphism that have been suggested to reflect differences in gendered
activities and behavior (Laffranchi et al., 2020; Saers et al., 2017; Temple et al., 2021; Zelazny et al., 2021). While these studies do not consider age-related changes and/or do not have sufficient sample sizes to do so, they do underscore the plasticity of bone morphology with behavior/lifestyle and do not support the “mismatch” hypothesis that females in modern human populations are predestined to have less robust bones or bone fragility.

3.2 Bioarchaeological studies of bone loss

Understanding the natural history of bone aging and fragility requires examination of the developmental interplay of nonmechanical influences (such as diet and reproduction) together with mechanical influences on skeletal robusticity. It is important to understand bone remodeling and modeling processes and how material properties of bone change dynamically during growth and aging if we are to interpret the static bone morphology observed in the archeological record (Agarwal & Beauchesne, 2011; Currey, 2003; Gosman et al., 2011). Several recent bioarchaeological studies, discussed below, have begun to do this and offer a more holistic picture of bone loss.

The classic studies of bone loss in Sudanese Nubia were the first to consider and compare bone growth and maintenance in both juvenile and adult skeletons. Armelagos et al. (1972) suggested that femoral cortical bone loss in young-aged female Nubians was likely due to early growth disturbance and stress experienced during pregnancy and lactation. A later study of cortical bone growth in juvenile Nubians from the Kulubnarti site found that while bone mineral content increased after birth, the process of modeling combined with likely periods of nutritional stress, caused a reduction in percent cortical area during early and late childhood (Van Gerven et al., 1985). More recently, Rewekant (2001) directly correlated developmental stress with variation in bone morphology through the examination of adult cortical bone loss with indicators of growth disturbance (specifically compression of the skull base and vertebral stenosis) in two Polish medieval populations with different socioeconomic statuses. Greater cortical bone loss was found in the population that also showed greater disturbance of bone growth during childhood, suggestive of a relationship between the disturbance of growth and the achievement of both peak bone mass, and later age- and sex-related patterns of bone loss (Rewekant, 2001). As suggested by epidemiological studies and studies in small-scale societies, reproductive behavior is a key factor that influences bone maintenance, and this has also been identified in the archeological record since the early Sudanese Nubian studies. Recent observations of low BMD in young female medieval skeletons from Denmark (Poulsen et al., 2001) and Norway (Mays et al., 2006; Turner-Walker et al., 2001) have continued to argue that this is a result of insufficient nutrition together with pregnancy and lactation stress. However, the key question is whether the influence of reproduction in young adulthood has impact on later adult bone mass and strength. In another study of a historical European skeletal sample, Vogel et al. (1990) found that female skeletons actually showed better trabecular connectivity when compared with modern populations, which these authors attributed to the benefits of historic practices of high parity. I have argued that the loss of bone during the reproductive years in women in the past was transitory, and that in many circumstances bone loss during reproduction would have little or no effect on long-term bone fragility in women who would have survived to old age (Agarwal, 2008; Agarwal et al., 2004; Agarwal & Grynpas, 2009; Agarwal & Stuart-Macadam, 2003). While influences such as nutrition, physical activity, and reproduction are critical to understanding bone growth and maintenance, it is equally important to understand the trajectories these influences take over the life course in each individual and community (Agarwal & Beauchesne, 2011; Fausto-Sterling, 2005). Just as in modern populations, it also remains important to understand how influences affect bone metabolism along the different areas and bony envelopes of the skeleton (Gosman et al., 2011; Peck & Stout, 2007; Robling & Stout, 2004).

The well-studied British medieval skeletal sample, Wharram Percy, illustrates the complex influences on bone morphology, maintenance, and fragility. Wharram Percy is a deserted rural medieval (11–16th centuries CE) village in North Yorkshire, England, and individuals buried at the site are thought to be ordinary peasants who lived in the agricultural settlement or elsewhere in the parish (Mays et al., 2007). A study of cortical bone loss in the hand (the 2nd metacarpal) and hip (femur) at Wharram Percy found age- and sex-related patterns of cortical bone loss to be similar to modern populations (Mays, 1996; Mays et al., 1998). A subsequent study by McEwan et al. (2004) examined BMD in the arm (the radius) in juvenile skeletons from the site in relation to indicators of growth disturbances attributed to poor nutrition (specifically cortical index [CI], Harris lines, and cribra orbitalia). BMD was found to be correlated with overall growth but not strongly correlated with the CI, the latter showing greater sensitivity to nutritional stress (McEwan et al., 2004). Both adults (of all ages) and children at Wharram Percy are believed to have relied heavily on
grains and likely endured periods of nutritional deficiency (Mays, 1999; McEwan et al., 2004). These studies support the assertions that long bone cortical thickness is strongly influenced by nutritional stress and that reduced long bone quantity during modeling can be carried into adulthood exacerbating the later loss of cortical bone density. However, study of trabecular quantity and quality in the vertebrae at Wharram Percy, found atypical patterns of bone loss, with bone loss observed in young-age females, and similar amounts of bone in both sexes into old age (Agarwal et al., 2004; Agarwal & Grynpas, 2009) (Figure 2). Although these patterns in vertebral bone density differ from the cortical results in the same sample, and are unusual when compared with the traditional paradigm of osteoporosis that emphasize bone loss postmenopause, they actually do concur in part with recent population-based epidemiological studies that emphasize different patterns of bone loss in trabecular and cortical tissue (Osterhoff et al., 2016). For example, recent longitudinal data on changes in BMD in the tibia (Lauretani et al., 2008) and multiple sites (radius, tibia, spine) (Riggs et al., 2008) using QCT both show substantial trabecular bone loss to occur in younger age. However, while trabecular bone loss in younger age is found at Wharram Percy, the medieval sample does not show the rapid and steep postmenopausal bone loss that is noted in the modern epidemiological studies (Lauretani et al., 2008; Riggs et al., 2008). Wharram Percy females do not show significantly lower vertebral bone density when compared with men in any given group. I have suggested that these patterns of bone turnover in the trabecular tissue could reflect reproductive practices at Wharram Percy. Based on historical evidence and nitrogen isotope data, we know that parity was high and breastfeeding duration (about one and a half to two years) was relatively long in the rural medieval population (Mays et al., 2007). Most young age women in the skeletal sample would have been pregnant or nursing at the time of death, thus, their bone loss likely reflects this status at the time of death (Agarwal et al., 2004; Agarwal & Grynpas, 2009; Mays et al., 2006). However, this loss of bone related to reproduction would have been transient and would not necessarily have negatively impacted long-term bone maintenance. Further, a lifetime of higher parity and longer periods of breastfeeding as compared to modern women would have created a different hormonal milieu for the rural women. Together with a likely later age of menarche and possibly earlier age at menopause, these reproductive practices would have resulted in a dynamic and lower lifetime steroid exposure in comparison to modern Western females, who give birth to fewer children and practice little or no breast-feeding (Pollard, 1999; Sperling & Yewoubdar, 1997). At menopause, the rural medieval women would not have suffered from the sudden loss of hormones and associated bone loss that modern women do, and the benefits of high parity and extended breastfeeding may have maintained their skeletons in old age to a similar degree as their male counterparts (Agarwal et al., 2004). Further, it is key to note there is little or no evidence for typical fragility fracture at Wharram Percy (McEwan et al., 2005). While cortical bone loss appears to reflect both nutritional impact on peak bone mass accrual compounded by aging, this loss does not appear to impact overall bone fragility and strength. It is also likely that physical activity would have been a key player in bone growth and maintenance in this population. Both sexes at Wharram Percy would have engaged in an arduous farming lifestyle (Mays et al., 2007). Moreover, documentary evidence indicates that rural medieval

FIGURE 2 Images of trabecular microarchitecture from human lumbar vertebrae. (A) From a younger individual. (B) Right from an older individual. Note the overall loss of trabecular elements in the older individual, with a preferential loss of horizontally oriented trabeculae, reducing the mechanical strength of the remaining vertical elements. The anisotropy of the trabecular architecture change occurs throughout the life cycle and contributes to the overall fragility of the bone. In many archeological samples, loss of trabecular bone is seen in young age individuals or in both sexes (see text). Images courtesy of Sabrina C. Agarwal.
peasants did not have a rigid sexual division of labor. The equally demanding physical lifestyles of rural men and women would have started early in life (Gies & Gies, 1981; Mays et al., 2007; McEwan et al., 2004), and this could have afforded both sexes biomechanical loading on bone tissue to sustain them through adulthood and into old age.

It is also noteworthy, that a subsequent study of trabecular bone loss in another medieval British archeological sample from an urban setting found different age- and sex-related patterns of bone loss (Agarwal, 2012). The study of bone loss in samples from the urban sites St. Nicholas Shambles and the Royal Mint, showed females to have less trabecular bone in old age, and significant sex difference in bone quantity and quality in old age (with female showing less bone as compared with males), patterns more similar to what is seen in modern populations (Agarwal, 2012). I have suggested that these patterns of bone loss reflect the specific reproduction and lifestyle behaviors of medieval women living in the urban setting, as compared to the rural setting of Wharram Percy. The types of activities and levels of activity would have been very different in the urban population, with medieval cities as the primary sites of craft production and most citizens involved in light labor, particularly as compared to rural farming-community inhabitants (Agarwal, 2012). Women in the urban setting would not have had the same arduous labor and biomechanical loading as the rural women from Wharram Percy, that would have afforded protection to their bone density (Agarwal, 2012). This suggestion has also been supported by a recent study of cortical bone loss in the foot that also compared rural and urban British archeological populations (Wilson et al., 2020). Further, although parity could have been conceivably similar in urban and rural women, urban women likely had shorter periods of breastfeeding and more common use of wet nursing (Gies & Gies, 1981). I have suggested, that the urban medieval women would have experienced chronically elevated hormonal levels that mirror modern women, and would have experienced the sudden change in hormonal exposure following menopause that can lead to a dramatic loss of bone (Agarwal, 2012). This could also partly explain the observation in the urban sample of significant difference in bone loss between the sexes in the oldest group. What is key to note, is that observed sex differences do not relate to inevitable biological sex-determined outcomes, but instead gendered behaviors that can vary in time and space. Differences in the reproductive gender roles for urban medieval women as compared to rural medieval women are directly related to their differing lifestyles. These differences in rural and urban populations mirror the dramatic and often biologically reproductive adaptive differences that have been observed between modern Western societies and rural non-Western societies, as discussed in evolutionary medicine (Trevathan, 2007; Valeggia & Ellison, 2001; Vitzthum, 2001). Here, the differences in bone loss observed in urban and rural archeological populations demonstrate the biocultural plasticity of reproductive functioning and the consequences of this flexibility to health. Further, the patterns of bone maintenance in both these medieval samples illustrate that bone loss and fragility of the skeleton is not constrained by the biological processes of senescence and menopause. Instead, the careful piecing of evidence on nutrition, reproductive practices, and activity patterns, together with the skeletal data across different bony envelopes, demonstrate how behaviors can influence bone loss across the life cycle. There have been many more studies of bone aging and osteoporosis in the archeological record (for detailed review see Agarwal, 2018), but the etiology of bone loss in the past remains variable (Agarwal, 2008; Agarwal & Grynpas, 2009). While some archeological samples show temporal and/or spatial patterns of bone loss, many do not, and many populations in the past show different patterns of bone loss and fragility than the normative patterns observed in modern Western populations (Agarwal, 2008). For example, bone loss in young age and in both sexes has been noted in other studies (Agarwal, 2012; Agarwal & Grynpas, 1996, 2009; Beauchesne & Agarwal, 2014; Beauchesne & Agarwal, 2017; Brodholt et al., 2021; Ekenman et al., 1995; Holck, 2007; Lees et al., 1993; Weaver, 1998), and age-related loss is also often very similar between the sexes in some populations (Agarwal et al., 2004; Brickley, 2002; Cho & Stout, 2011; Ekenman et al., 1995; Holck, 2007; Wilson et al., 2020). These patterns often deviate from industrialized populations, and reflect context specific influences of lifestyle and activity patterns. Fragility fractures in the past also seem to occur at far lower frequencies than in modern populations (Agarwal, 2008; Ives et al., 2017). Finally, studies that examine age- and sex-related patterns of bone loss across the skeleton (e.g., Beauchesne & Agarwal, 2017) are able to demonstrate the fluid patterns of bone loss across the different remodeling cortical and trabecular envelopes.

Admittedly, studies of bone health in the archeological record can be problematic. Bioarchaeological studies, like retrospective epidemiological studies, are cross-sectional in nature, and thus any particular measure of bone is a snapshot in time. Larger sample sizes can help mitigate some of the limitations of cross-sectional studies. However, mortality samples also suffer from demographic bias with incomplete or biased skeletal samples. Selective mortality and
frailty (DeWitte & Stojanowski, 2015; Wood et al., 1992) are potential confounding factors in all bioarchaeological mortality samples. The use of multiple lines of evidence is important to deal with potential bias, as a convergence of data from different measures partially controls for some of the effects of selective mortality and frailty (DeWitte & Stojanowski, 2015; Wright & Yoder, 2003). Strong historic contextualization and biocultural approaches are also needed to understand biological data derived from archeological populations, such as a population’s diet, weaning practices, and association of health indicators with demographic patterns, to effectively consider hidden heterogeneity and its effects on selective mortality (DeWitte & Stojanowski, 2015; Wright & Yoder, 2003). Another concern in the interpretation of age-associated diseases in archeological samples is the issue of life expectancy in the past. However, low life expectancy in the past is also related to high infant mortality (as opposed to differences in longevity), and according to historical records and estimates, individuals having survived infancy would have had a good possibility of living to an old-enough age to suffer bone loss (Agarwal, 2012). Finally, bioarchaeological analysis faces issues related to the accuracy of estimating age-at-death from the skeletons of older individuals after about 60 years of age (Agarwal, 2012). Although life expectancy in the past and age-estimation could limit our ability to separate osteoporosis in the oldest groups related to senile bone loss, it should not limit our ability to see changes in bone maintenance in younger adult age, particularly following menopause. The variable patterns of bone maintenance fragility in the past should not be surprising given that groups in the past would have had very different biocultural histories from our own (Agarwal & Beauchesne, 2011). Bone maintenance and loss is the result of ontogenetic processes over the life cycle, with trajectories of bone maintenance laid out in early growth, refined during adulthood, and played out and modified within the everyday individual and generational choices of behavior and life experience (Agarwal & Beauchesne, 2011) (Figure 3). This approach views plasticity as more than adaptation to specific environmental contexts, and instead as a developmental process where plasticity is seen as constructing the body and skeleton over the life cycle and potentially over generations of multiple life cycles, as suggested by the developmental systems theory (DST) (Agarwal & Beauchesne, 2011; Fausto-Sterling, 2005; Oyama, 2000; Oyama et al., 2003). Archeological samples that allow us to assess this bone plasticity and development as measures of bone quantity and quality are direct products of the lived experience of the skeletal body crafted at the cellular level through bone remodeling.  

### 4 MOVING PAST STEREOTYPICAL INTERPRETATIONS OF BONE LOSS

The variability in bone loss across human populations in the past and the present suggests that models of normative bone loss that give primacy to senescence or menopausal hormonal depletion offer an incomplete understanding of skeletal aging. The use of life course models or a developmental-systems approach to understand bone loss is supported by recent biomedical and epidemiological studies on BMD and loss. Infant and adolescent growth spurts have been shown to be influential in defining later adult bone quality and quantity (Cooper et al., 2002, 2006; Gale et al., 2001; Javaid et al., 2006; Miller, 2005). While peak bone mass is generally thought to be heritable, it has been argued that heritability measures of bone mass or density are as fluid as age, height, gender, and body composition, and vary with environmental context (Seeman, 1997). Cooper et al. (2006) have suggested that fetal programming along with environmental cues early in life interact with the genome to create the boundaries of growth and development for a given individual. Fetal programming by maternal undernutrition has been shown to be a risk factor for low birth weight (Cooper et al., 2002), and low birth weight is strongly correlated with lower levels of basal growth hormones placing individuals at risk for lower peak bone mass, reduced mineralization, and an elevated rate of bone loss later in life (Cooper et al., 2002; Dennison et al., 2005). Further, a number of studies have shown that impaired fetal and childhood growth place individuals at risk for fragility fractures later in life (Dennison et al., 2005; Gale et al., 2001; Javaid et al., 2006). Reproductive behaviors, diet and nutrition, and levels of physical activity are then layered on these early life influences. While the study of bone loss in living small-scale societies and rural populations have utilized a *life history* theoretical approach, rather than a *life course* approach, they also call for more complex causal interpretations of bone loss. Yet even these studies have not found a clear normative picture of bone aging. The study of bone density in the forager-horticulturalist populations discussed earlier, the Tsimane and the Shuar, both emphasize that a combination of life experiences shape bone health later in life. However, the Tsimane show an association between early reproductive behavior and postmenopausal bone density, while Shuar postmenopausal bone density does not show an association (Madimenos, 2015; Madimenos et al., 2011; Madimenos et al., 2020; Stiegltz et al., 2015, 2016). Another study of BMD in women from...
FIGURE 3  A diagrammatic model of plasticity in the development and maintenance of the skeleton over the life course. Bone
maintenance and loss is the result of ontogenetic processes over the life course, with trajectories of bone maintenance laid out in fetal life and childhood, refined during adulthood, and played out and modified within each individual and potentially generations stages (represented as two-way arrows between circles). Circles represent major periods in the biological life cycle (fetal life, childhood and adolescence, young adulthood, and middle/old age) each containing examples of some of the major influences within each life stage that determine bone strength. Influences in each stage are cumulative and dependent on influences in earlier life stages. Cumulative influences shape overall skeletal morphology (depicted as the different size/shape skeletons in the center). Influences across the life cycle are dependent on the individual and community milieu (such as sex/gender, socioeconomic status, cultural, or community buffers) (figure adapted from Agarwal & Beauchesne, 2011)
rural Poland found that body size and habitual use were more correlated with cortical BMD than reproductive life history traits (Lee et al., 2021). Finally, a recent life history study of long bone strength and cross-sectional size in premenopausal industrial European women found that greater maternal investment (as measured by higher birth weight) and slower maturation rate (as measured by later age at menarche) was associated with larger and more mechanically competent long bones (Macintosh et al., 2017). However, this study also found physical activity during later life to be one of the main determinants of adult bone strength, particularly in certain long bones, that highlights the continuing plasticity of the skeleton even within trajectories of growth determined by early life history. While the goal of these studies has been to discover unifying influences on bone strength and maintenance, they instead highlight the complex synergistic relationship of early life history influences with later lifestyle behaviors.

The goals of this article were to raise a call to consider the cumulative and fluid biocultural influences on the skeleton over the life course, and to reflect on which measures of bone loss in the different parts of the skeleton are actually biologically and/or socially meaningful. These two considerations actually go hand in hand, as the best way to get at the complex influences on bone maintenance over the life cycle is to consider multiple measures. The varying and complex patterns of bone loss between the sexes, as seen in the studies from medieval Wharram Percy (Agarwal et al., 2004; Agarwal, 2016; Agarwal & Grynpas, 2009; Mays, 1996; Mays et al., 1998; McEwan et al., 2005), or the Roman sample from Velia (Beauchesne & Agarwal, 2017), only emerge when bone remodeling is viewed across the skeleton and analyzed together. Interpreting measures in a meaningful way requires population and individual-level contextualization, and is best conducted with as much knowledge of wider population patterns of growth and health. Several notable studies have attempted to consider both systemic and mechanical influences on bone structure and biology. For example, a study by Temple et al. (2014) compared skeletal growth and stress between Early Neolithic and Late Neolithic foragers from Cis-Bakal, Eastern Siberia (by examining stature, cortical thickness, and medullary width). They found that while the Early Neolithic sample showed skeletal evidence for systemic stress (stunting in femoral length and wasting in body mass) they showed no difference from the later Neolithic sample in cortical bone measures (Temple et al., 2014). The authors suggest that biomechanical stress may still have been sufficient in the early Neolithic despite systemic stress affecting growth (Temple, 2014). Similarly, Schug and Goldman (2014) attempted to examine midshaft femoral bone morphology along with another indicator of bone turnover in the study of stress in a second millennium BC prehistoric sample of immature skeletons from India. The authors found that while immature femora show cross-sectional bone shape that is consistent with the acquisition of locomotor behavior, they also show reduced compact bone mass consistent with a significant increase in cortical bone porosity and low BMI (Schug & Goldman, 2014). Here the extreme effects of wasting and poor health on bone growth and metabolism could have had long-term effects on adult bone morphology and health (Schug & Goldman, 2014). Another study by Rewekant (2001) in two Polish medieval populations also correlated growth patterns and developmental stress with variation in skeletal morphology and bone loss, finding greater metacarpal cortical bone loss in the population that also showed greater disturbance of bone growth and achievement of peak bone mass. Finally, studies that scale between both population-level patterns of bone loss and individual contextualized histories (such as bone loss in women who clearly died in birth/pregnancy) (Agarwal et al., 2015) also offer more nuanced interpretation of bone loss. These types of studies are important in elucidating the complex interplay of systemic and mechanical influences on bone strength, morphology, and quality over the life course.

Not all measures of bone quantity and loss across the skeleton are commensurate. As seen in this review, some bones are better gauges of biomechanical signatures (such as long bones like the femur or tibia), whereas other bones are better gauges of multifunctional or metabolic signatures (such as the trabecular filled bones of the ribs or vertebrae). Both studies of small-scale/rural populations and archeological samples, continue to base interpretations on the assumption that bone loss equals risk of overall skeletal fragility, even when bone loss is observed in only one location of the body. While bone loss in modern industrial populations is assumed to predispose to fracture risk based on clinical T-score estimates, as discussed earlier, skeletal/tissue location of reduction in bone quantity and aspects of bone quality are equally fundamental to determining bone strength. In trying to answer the question of which measures are most biologically or social meaningful, researchers first need to pivot to ask at what point does bone loss actually matter? Studies of diachronic changes in bone geometry have been important in highlighting the gracilization of the human skeleton thorough time, and offer a methodological way to assess subsistence strategies and infer mobility in paleontological samples. However, without evidence for increased fragility (such as mechanical failure of bone or fracture) why does reduced bone loss matter? The evolutionary hypothesis of “mismatch” and
predisposition to fragility is not supported by the now numerous studies that show variability in bone density and strength in time and space. How do we know reduction in bone density is not just a signal of adaptation or adjustment to specific environmental contexts? How can we know if bone loss occurred in many instances in the past but fluctuated during the lifespan? How can we see if compensatory mechanisms in other aspects of bone maintenance also took place? These questions are challenging to answer with cross-sectional studies, but tackling them is potentially possible with biocultural and life course approaches that methodologically examine bone loss with different measures.

Finally, we might ask, if there is growing evidence that bone growth and health is clearly influenced by multiple factors over the life cycle, why is the normative model of bone loss across age and sex still so pervasive? Bioarchaeological and evolutionary studies of bone loss are still largely based on the biomedical a priori expectation that biological sex is the primary predictor of bone fragility. I argue that this gender ideological bias is present from the study design stage to data interpretation, and is an obstacle to realizing the full potential of life-course approaches to bone morphology and health. Much of this begins with the fundamental conflation of the influences of biological sex versus influences of gender (Agarwal, 2012). For example, diachronic and evolutionary models of bone morphology highlight an expectation for “sexually dimorphic” differences due to female physiology but fail to appreciate the widely different trajectories that gendered behavior can have on this physiology and its influence on bone morphology in the first place. These studies highlight sex steroids as the primary influence on dimorphic differences (Saers et al., 2017). Further, non-mechanical influences on bone maintenance are generally characterized as “confounding variables” layered on signatures of mechanical loading, and stated hypotheses on sexual dimorphism in bone density typically have the expectation that males will have more robust structures as compared to females (Doershuk et al. 2019; Mulder et al. 2020; Scherf et al., 2016; Saers et al., 2017). Studies continue to note it “surprising” when sex differences in bone structure/quality are not found (Mulder et al. 2020) or “striking” when females show greater bone density than males in the past (Saers et al., 2017). In bioarchaeological studies the assumption that the greatest determinant of bone health is biological sex is so pervasive, that in many instances studies only examine bone loss in the females in a given population (e.g., Mays, 2000). Even in biocultural models, environmental and cultural effects on skeletal maintenance and bone loss are often viewed as only potential modifiers that are still tightly constrained by biology. As such, indications of bone loss or osteoporosis in the past are generally regarded to reflect the irreversible course of menopause and aging (Macho et al., 2005; Mays, 1996; Mays et al., 1998; Turner-Walker et al., 2001). However, the assertion that the patterns and prevalence of osteoporosis in the past is the same as in modern populations (Curate, 2014; Mays et al., 1998; Rosen, 1999; Turner-Walker et al., 2001) is untrue. Studies in small-scale societies which utilize life history theory are also designed with the assumption that biological sex is the primary determinant of bone fragility. For example, while both men and women among the Tsimane forager-horticulturalists of Bolivia show equal age-related bone loss and reduced bone status (Kraft et al., 2020; Stieglitz et al., 2016), findings of bone loss in the females are presented and interpreted separately as reflecting greater cumulative reproductive burden (Stieglitz et al., 2015), despite the fact that both sexes (particularly males) show greater bone loss than industrialized counterparts. Similarly, in their study of bone loss in rural Poland, Lee et al. (2021) examine bone loss only in females, without consideration of male bone health in the population.

While the focus on females in these studies is logical as their interest lies in reproductive stress, they potentially miss the identification of larger cross-cutting variables with age and sex that could affect bone maintenance in these populations over the life cycle.

These expectations and assumptions must be held in question when so many bioarchaeological studies have reported variable sex-related patterns of cortical and trabecular density (Agarwal, 2008, 2012; Agarwal, 2018). Some recent studies of bone robusticity have begun to shift the focus to female patterns of strength and gendered patterns of labor, not just fragility with age. For example, the recent study by Macintosh et al. (2017) confirmed that while female prehistoric Central European agriculturalists did not show the same temporal changes as males in lower limb strength, they did show exceptional upper limb strength (more than even modern female athletes) due to intense manual labor during life (Macintosh et al., 2017). Other bioarchaeological studies of bone robusticity have also challenged the dominant perception that males are biologically destined to have stronger upper bodies than females, with various prehistoric populations showing instances where females develop even stronger limb bones than male peers (Miller et al., 2018; Ogilvie & Hilton, 2011; Wescott & Cunningham, 2006), even in the face of significant bone loss on other cortical envelopes (Miller, 2016).

Lastly, researchers must expand out of their silos of focus and expertise. Researchers examining sex differences in robusticity and bone loss in paleontological samples, and in small-scale or rural living societies, would benefit from consideration of bone material properties along with the
different envelopes and consideration of mediators of bone maintenance outside of biomechanical stress, and particularly explore the large number of bioarchaeological and contextualized studies of bone remodeling and maintenance that have done this. Similarly, clinical studies of bone loss can benefit from the deep temporal perspective of archeological studies. While bone loss and osteoporosis cause increasingly significant morbidity and mortality in Western industrialized populations, the normative statistical and sex-related pattern of bone loss and fragility does not fit all global populations or individuals. Data from developing and historical populations show varying patterns of bone loss that are not easily explained by biological sex and aging alone, and instead vary across the life course.

There has been a call to better understand sex differences in health outcomes by focusing on the scientific study of the interaction of sex and gender variables (Richardson et al., 2015), and recent federal NIH policy and granting mandates aim to include wider age, gender and ethnic diversity in research. Bioarchaeological studies of bone loss have been conducted in almost all temporal periods and geographical locations of human populations, and offer an invaluable resource to examine the nexus of bone health across the life cycle in groups that have lived a variety of lifestyles. Studies that seek to fit their study design or data to stereotypical views of bone fragility are missing this opportunity. More importantly, our narratives and language are important. Studies of bone loss that focus language on reproductive trade-offs, disposable soma, poor maternal investment, mismatched bodies, or confounding variables, inadvertently frame women’s bodies within the confines of sex steroids and as solely reproducers, predestined to physiological and/or structural failure, and further reify binary sex differences in human health. Instead, anthropological studies in historic and contemporary populations should leverage their vantage point to showcase and explore variation over the life course and plasticity in aging experiences.

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Sabrina C. Agarwal: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration.

CONFLICT OF INTEREST
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ENDNOTES
1 A life history approach emphasizes the use of life history theory. According to life history theory, metabolic resources at any stage of the life cycle must be allocated across four competing functions: growth, reproduction, maintenance, and defense or avoiding death. Variation in these life history allocations are evolutionarily derived strategies to promote increased reproductive fitness. Life history strategies are not conscious or planned outcomes at the individuals or population group level, but constitute biological/behavioral traits which evolved through a series of trade-offs, meaning greater allocation of resources to one function results in less energy being available for the others. As such, life history approaches suggest that phenotypes (such as bone morphology or bone loss) can be the result from tradeoffs in energy allocation between growth, maintenance, and reproduction.

2 Life course approaches broadly emphasize the role of physical and social exposures during gestation, childhood, adolescence, young adulthood, and later adult life (e.g., the development and physical manifestations of disease risk). The focus is on biological, social, and psychosocial pathways that operate over the life course, as well as across generations. Life course approaches to bone loss are situated in developmental systems theory (DST). In DST development and phenotype of an organism is considered contingent on context (broadly environment) and can extend well into postnatal growth. The interaction of developmental influences is key, and developmental information is thought to reside in the interaction of genes and environment (including non-gene factors such as ecological and social resources, and other epigenetic processes).

REFERENCES


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19 of 23


Lancet, 341(8846), 673–675.


Archives of Internal Medicine, 167(15), 1641–1647. https://doi.org/10.1001/archinte.167.15.1641


Vintage.


Osteoporosis International, 6(2), 153–159.


Science Advances, 3(11), eaao3893. https://doi.org/10.1126/sciadv.aao3893


PLoS One, 9(11), e112116. https://doi.org/10.1371/journal.pone.0112116


UC Berkeley. Retrieved from. https://escholarship.org/uc/item/9c000hec#author


